CLAIMS

We claim:

1.   A method of diffractometrically resolving a structure of a crystal by obtaining an
5   electron density distribution of the crystal, the method comprising:

          obtaining X-ray diffraction data reduced to intensities corresponding to centric
and acentric reflections;

10   using the intensities corresponding to the centric reflections to estimate a noise
level of the X-ray diffraction data;

          using the intensities corresponding to the acentric reflections to obtain an
observed anomalous signal of the X-ray diffraction data;

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          calculating an anomalous scattering signal corrected for noise;

          calculating a ratio of said anomalous scattering signal corrected for noise to
said noise level; and

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          calculating an anomalous scattering power of the crystal;

          wherein said anomalous scattering signal corrected for noise is used to calculate the
electron density distribution and to resolve said structure of said crystal.

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2.   A method of determining an electron density distribution of a crystal, said method
comprising the steps of:

          collecting X-ray diffraction data comprising intensities corresponding to a
30   centric reflection pair and an acentric reflection pair;

subtracting the intensities of said centric reflection pair to obtain a first

intensity difference;

subtracting the intensities of said acentric reflection pair to obtain a second

5   intensity difference;

calculating an anomalous scattering signal corrected for noise using said first

intensity difference and said second intensity difference; and

10   using said anomalous scattering signal corrected for said noise to determine an

electron density distribution for the crystal.

3.   The method of claims 2 wherein said first intensity difference is a measurement of the

noise level in the X-ray diffraction data.

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4.   The method of claims 2 wherein said second intensity difference is a measurement of

the anomalous scattering signal plus noise level in the X-ray diffraction data.

5.   A method of determining an electron density distribution of a crystal, said method

20   comprising the steps of:

collecting X-ray diffraction data comprising intensities corresponding to a

plurality of centric reflection pairs and a plurality of acentric reflection pairs;

25   subtracting the intensities of said plurality of centric reflection pairs to obtain a

plurality of first intensity differences and calculating an average first intensity

difference;

subtracting the intensities of said plurality of acentric reflection pairs to obtain

30   a plurality of second intensity differences and calculating an average second intensity

difference;

calculating an anomalous scattering signal corrected for noise using said average first intensity difference and said average second intensity difference; and

using said anomalous scattering signal corrected for said noise to determine an electron density distribution for the crystal.

6. The method of claims 5 wherein said average first intensity difference is a measurement of the noise level in the X-ray diffraction data.

7. The method of claims 5 wherein said average second intensity difference is a measurement of the anomalous scattering signal plus noise level in the X-ray diffraction data.

8. The method of claim 5 further comprising the step of calculating a first weighted average of the first intensity difference by dividing said average first intensity difference by the standard deviation of said intensities and calculating a second weighted average of the second intensity difference by dividing said average second intensity difference by the standard deviation of said intensities.

9. The method of claim 5 further comprising the step of calculating a ratio of said first weighted average of the first intensity difference and said second weighted average of the second intensity difference.

10. The method of claim 9 further comprising the step of calculating a first weighted average of the first intensity difference by dividing said average first intensity difference by the square of the standard deviation of said intensities and calculating a second weighted average of the second intensity difference by dividing said average second intensity difference by the square of the standard deviation of said intensities.

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11.   The method of claim 10 further comprising the step of calculating a ratio of said first weighted average of the first intensity difference and said second weighted average of the second intensity difference.

5   12.   The method of claims 2 or 5 further comprising the step of using said anomalous scattering signal corrected for said noise to determine an anomalous scattering power of said crystal.

       13.   The method of claims 1, 2 or 5 wherein the crystal comprises a material selected from
10   the group comprising: a protein; a peptide; a protein - protein complex; a protein - lipid complex; an olignucleotide; a carbohydrate; a lipid - carbohydrate complex and a nucleic acid - protein complex.

       14.   A method of monitoring changes in the signal-to-noise ratio of X-ray diffraction data,
15   said method comprising the steps of:

              measuring a first set of intensities corresponding to a plurality of centric reflection pairs and a plurality of acentric reflection pairs and calculating an first anomalous scattering signal-to-noise ratio for said first set of intensities;

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              measuring a second set of intensities corresponding to a plurality of centric reflection pairs and a plurality of acentric reflection pairs and calculating a second anomalous scattering signal to noise ratio for said second set of intensities; and

25   comparing said first anomalous scattering signal-to-noise ratio to said second anomalous signal-to-noise ratio.

       15.   The method of claim 14 wherein said first and second anomalous scattering signal-to-noise ratios are governed by the expression:

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$$Ras = \frac{\Delta a}{\Delta c}$$

wherein Ras is the anomalous scattering signal-to-noise ratio, Δc is the ratio of the average intensity difference for said centric reflection pairs to the standard deviation of said intensities and Δa is the ratio of the average intensity difference for said acentric reflection pairs to the standard deviation of said intensities.

16.   The method of claim 14 wherein said first and second anomalous scattering signal-to-noise ratios are governed by the expression:

$$Ras = \frac{\Delta a}{\Delta c}$$

wherein Ras is the anomalous scattering signal-to-noise ratio, Δc is the ratio of the average intensity difference for said centric reflection pairs to the square of the standard deviation of said intensities and Δa is the ratio of the average intensity difference for said acentric reflection pairs to the square of the standard deviation of said intensities.

17.   A method of collecting X-ray diffraction data, said method comprising the steps of:

measuring intensities corresponding to a plurality of centric reflection pairs and a plurality of acentric reflection pairs;

calculating anomalous scattering signal-to-noise ratios for said intensities corresponding to a plurality of data collection time intervals; and

stopping the collection of said intensities when said anomalous scattering signal-to-noise is below an anomalous scattering signal-to-noise threshold.

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18. The method of claim 17 wherein said anomalous scattering signal-to-noise threshold is 1.67.

19. A method of increasing the anomalous scattering signal-to-noise ratio of X- ray diffraction data, said method comprising the steps of:

dividing said X-ray diffraction data into a plurality of discrete sub-groups corresponding to different collection time intervals;

calculating the anomalous scattering signal-to-noise ratio of each of said discrete sub-groups; and

combining two or more merged subgroups, thereby generating a combined X-ray diffraction data set having an anomalous scattering signal-to-noise ratio greater than the anomalous scattering signal-to-noise ratios of said merged subgroups.